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Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

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Ladies and Gentlemen:

Subject: Notice in Accordance with Section 8(e) of TSCA - Preliminary Results of a 90-Day Drinking Water Study of 2-Pyrrolidone - Reference EPA Document Control Number 8EHQ-1089-0829.

In accordance with the requirements of reporting under the Toxic Substances Control Act, Section 8(e), International Specialty Products (ISP) and BASF Corporation are submitting the following preliminary data on a 90-day drinking water study in rats supplementing EPA's existing 8(e) file on 2-pyrrolidone (8EHQ-1089-0829).

2-Pyrrolidone was administered to groups of 10 male and 10 female Wistar rats at doses of 0 ppm (test group 0), 600 ppm (test group 1), 2,400 ppm (test group 2), 7,200 ppm (test group 3), and 15,000 ppm (test group 4) in the drinking water over a period of 3 months to determine the toxicological profile and the no observed adverse effect level (NOAEL).

Food consumption, water consumption and body weight were determined each week. The animals' state of health was checked each day. When the animals were weighed, they were subjected to an additional comprehensive clinical examination.

Ophthalmological examinations were carried out in the animals of the control group and highest dose group prior to the start and toward the end of the administration period.

Urinalysis, clinicochemical and hematological examinations were carried out in all animals toward the end of the administration period.

All animals were subjected to gross-pathological assessment, followed by a comprehensive histopathological examination of all control and top dose animals. Gross lesions, thymus, lungs, liver, kidneys, adrenals and stomach were examined histopathologically in all groups.

The following substance-related findings were obtained:

Water consumption was decreased in males and females of test group 4 and in females of test group 3. Food consumption and body weight development were also impaired in these groups, most probably as a consequence of the decreased water consumption.

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There were a number of statistically significant changes in clinical chemistry parameters for rats receiving 2-pyrrolidone relative to the corresponding control groups. Most of these changes were considered to be unrelated to test compound intake, since they were generally mild, showed no dose-response relationship and occurred inconsistently between sexes.

In contrast, the following changes in test groups 4 and 3 appeared to be treatment related: prolonged prothrombin time, decreased total protein and globulins, increased triglycerides, and decreased creatinine and, in male animals, a reduction of urinary volume, an increased urinary specific gravity and a dark yellow discoloration of urine. All of these changes are probably consequences of the reduced intake of drinking water, the reduced food consumption or the reduced body weights. None of the aforementioned clinical chemistry and urinary changes are considered to be toxicological responses per se.

Organ weight determination revealed increased relative kidney weights in males and females of test group 4 and in males of test group 3. Although there was no histological correlate to these weight changes, a treatment-related effect cannot be ruled out.

Alteration of the cellular composition of the thymic cortex was observed in treated females; it did not occur in control females or in any male animal. The finding was characterized by thymocytes with an irregular size and shape and an increased number of large, pale-staining, blast-like lymphocytic thymocytes that were interdispersed among smaller, dark staining cells. A clear dose-response relationship in the incidence of the lesion could not be established. No change was seen in the cortex/medulla ratio and in the thymic medulla, nor in any other T-cell areas of other organs examined (e.g. spleen, mandibular and mesenteric lymph nodes, GALT, bone marrow). In addition, no obvious deviations were recorded from the differential white blood count or other hematological parameters.

This type of finding is new to us and the toxicological significance of its isolated occurrence in female rats is not yet known.

Please note that this letter does not contain any confidential business information. If you have any further questions, please do not hesitate to contact me at (313) 246-6207.

Very truly yours,

BASF CORPORATION

Edward J. Kerfoot

Edward J. Kerfoot. Ph.D.
Director, Toxicology & Product Regulations

cc: Dr. J. Ansell
ISP Management Company, Inc.

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